

Fig. 1

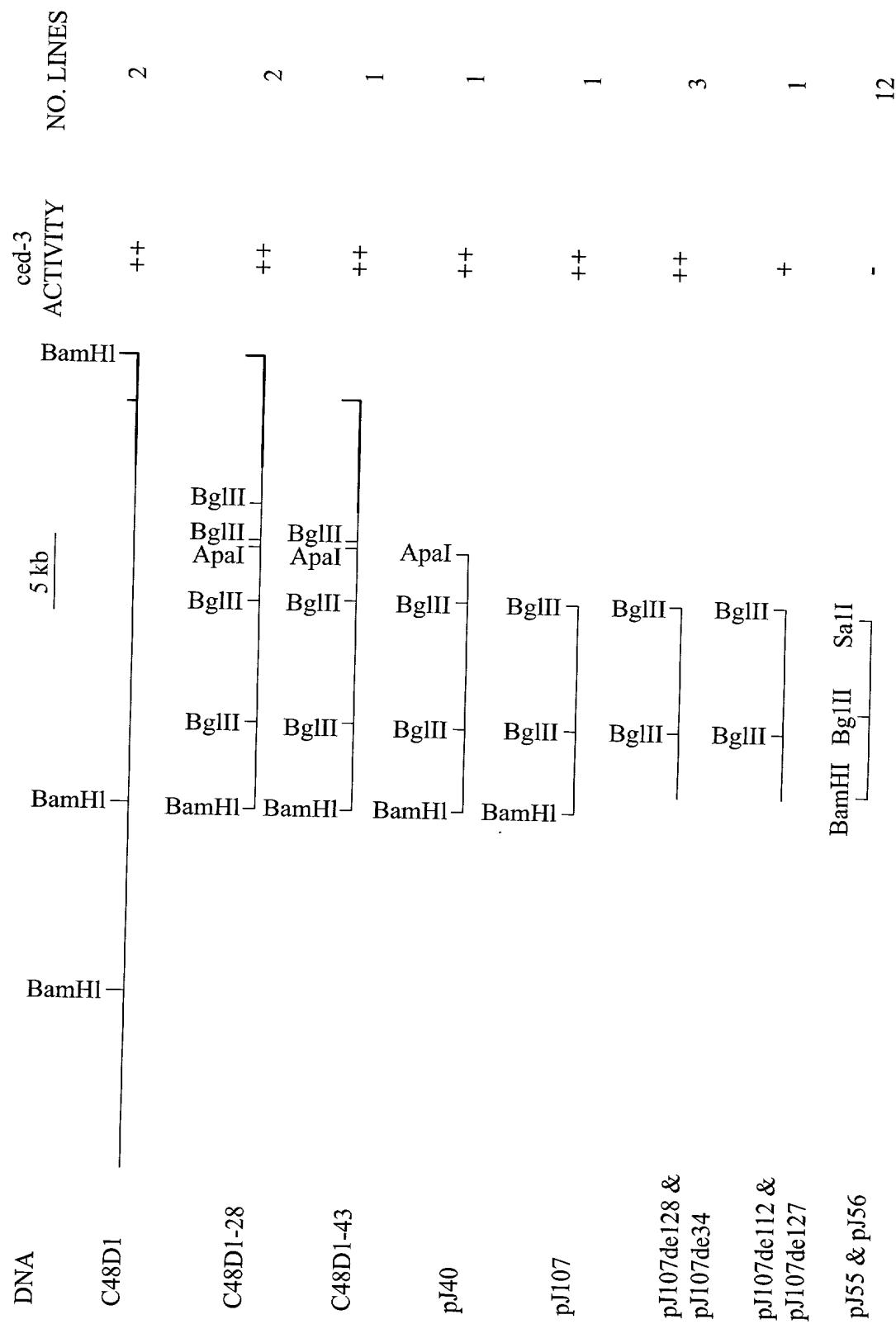


Fig. 2

ced-3 Genomic Sequence

AGATCTGAAATAAGGTGATAAATTAAATAAGTGTATTCTGAGGAATTGACTGT
 1 -----+-----+-----+-----+-----+-----+ 60
 TTTAGCACAATTAAATCTGTTCAGAAAAAAAGTCCAGTTCTAGATTTCCGTCTTA
 61 -----+-----+-----+-----+-----+-----+ 120
 TTGTCGAATTAAATATCCCTATTATCACTTTCATGCTCATCCTCGAGCGGCACGTCTC
 121 -----+-----+-----+-----+-----+-----+ 180
 AAAGAATTGTGAGAGCAAACGCGCTCCCATTGACCTCCACACTCAGCCGCAAAACAAAC
 181 -----+-----+-----+-----+-----+-----+ 240
 GTTCGAACATTCTGTGTGCTCCTTCCGTATCTGCAGTCATCTTGTGTT
 241 -----+-----+-----+-----+-----+-----+ 300
 TTTTCTTGTCTTTGTTGAACGTGTTGCTAAGCAATTATTACATCAATTGAAGAAA
 301 -----+-----+-----+-----+-----+-----+ 360
 GGCTCGCCGATTATTGTTGCCAGAAAGATTCTGAGATTCTCGAAGTCGATTTATAATA
 361 -----+-----+-----+-----+-----+-----+ 420
 TTTAACCTGGTTTTGCATTGTTGTTAAAAAAACCACTGTTATGTGAAAAACGA
 421 -----+-----+-----+-----+-----+-----+ 480
 TAGTTTACTAATAAAACTACTTTAAACCTTACCTCACCGCTCCGTGTTCATG
 481 -----+-----+-----+-----+-----+-----+ 540
 GCTCATAGATTTCGATACTCAAATCCAAAAATAATTACGAGGGCAATTAAATGTGAAA
 541 -----+-----+-----+-----+-----+-----+ 600
 CAAAAACAATCCTAAGATTCCACATGTTGACCTCTCCGGCACCTCTTCTTAGCCCC
 601 -----+-----+-----+-----+-----+-----+ 660
 ACCACTCCATCACCTCTTGGCGGTGTTCTCGAAACCCACTTAGGAAAGCAGTGTAT
 661 -----+-----+-----+-----+-----+-----+ 720
 CTCATTGGTATGCTCTTCGATTTATAGCTTTGTCGAATTCAATGCTTAAAC
 721 -----+-----+-----+-----+-----+-----+ 760
 AATCCAAATCGCATTATATTGTCATGGAGGCAAATGACGGGGTGGAACTTAGATGA
 781 -----+-----+-----+-----+-----+-----+ 840
 GATCAGGAGCTTCAGGGTAAACGCCCGGTCATTTGTACCACTTCATCATTTCC
 841 -----+-----+-----+-----+-----+-----+ 900
 GTCGTCTGGTATCCTCAACTTGTCCGGTTTGTTCGGTACACTCTCCGTGATGC
 901 -----+-----+-----+-----+-----+-----+ 960
 CACCTGTCTCCGTCCTCAATTATCGTTAGAAATGTGAACGTCCAGATGGGTGACTCATA
 961 -----+-----+-----+-----+-----+-----+ 1020
 TTGCTGCTGCTACAATCCACTTCTTCTCATGGCAGTCTTACGAGCCCATCATAAAC
 1021 -----+-----+-----+-----+-----+-----+ 1080
 TTTTTTCCCGAAATTGCAATAAACCGGCCAAAACCTTCTCCAAATTGTTACGCAA
 1081 -----+-----+-----+-----+-----+-----+ 1140
 TATATACAATCCATAAGAATATCTCTCAATGTTATGATTCTCGCAGCACTTCTCT
 1141 -----+-----+-----+-----+-----+-----+ 1200
 TCGTGTGCTAACATCTTATTTATAATATTCCGCTAAATCCGATTTGAGTATTA
 1201 -----+-----+-----+-----+-----+-----+ 1260
 ATTATCGAAAATTATCATAATAGCACCGAAAACACTAAAGGTAAAAGCTCCTT
 1261 -----+-----+-----+-----+-----+-----+ 1320

Repeat 1

=====
 TAAATCGGCTCGACATTATCGTATTAAGGAATCACAAAATTCTGAGAATGCGTACTGCGC
 1321 -----+-----+-----+-----+-----+-----+ 1380
 =====
 AACATATTGACGGCAAATATCTCGTAGCGAAAACACTACAGTAATTCTTAAATGACTAC
 1381 -----+-----+-----+-----+-----+-----+ 1440

Fig. 3

Fig. 3 (cont.)

5/24
A(n718)

2461 AGATCGTGAAGCAGTGCAACGACGGGGAGATGTGGCGTTGACGCCTTATGATGCTC
 I V K A V Q R R G D V A F D A F Y D A L
 60 70
 2520 | intron 2
 2521 TTCGCTCTACGGACACGAAGGACTTGCTGAAGTTCTGAACCTCTGCCAGATCGTAGG
 R S T G H E G L A E V L E P L A R S
 80 90
 2581 TTTTAAAGTTCGCGCAAAAGCAAGGGCTCACGGAAAAAGAGGCGGATCGTAATTT
 GCAACCCACCGGCACGGTTTCTCCGAAATCGAAATTATGCACTTCCAAATAT
 2641 TTGAAGTGAATAATATTTATTTACTGAAAGCTCGAGTGATTATTTATTTAACACTA
 2701 ATTTCTGGCGCAAAAGGCCATTTGTAGATTGCCGAAAATACTTGTACACACAC
 2761 ACACACATCTCCTCAAATATCCCTTTCCAGTGTGACTCGAATGCTGTCGAATTG
 2821 V D S N A V E F E
 100
 2880
 2881 GTGTCCAATGTCACCGGCAAGCCATCGTCGGAGCCGCGCATTGAGCCCCGCCGGCTACAC
 C P M S P A S H R R S R A L S P A G Y T
 110 120
 2941 TTCACCGACCCGAGTTACCGTGACAGCGTCTTCAGTGTCAATTCACTTCTTATCA
 S P T R V H R D S V S S V S S F T S Y Q
 130 140
 3001 GGATATCTACTCAAGAGCAAGATCTGTTCTGATCGCGTGCATTCACTCGGATCG
 D I Y S R A R S R S R S R A L H S S D R
 150 1 60
 3061 | intron 3
 ACACAATTATTCACTCTCCAGTCACGCATTCCAGCAACCTTGATGTTGATGCG
 H N Y S S P P V N A F P S Q P S
 170
 3121 Repeat 1
 AACACTAAATTCTGAGAATGCGCATTACTAACATATTGACGCGAAATATCTCGTAGC
 3181 GAAAAATACAGTAACCCCTTAAATGACTATTGAGTGTGCGATTACGGGCTCGATTTTCG
 3240

Fig. 3 (cont.)

==>
 AAACGAATATATGCTCGAATTGTGACAACGAATTAAATTGTCACTTTGTGTTTCTT
 3241 -----+-----+-----+-----+-----+-----+ 3300

Repeat 1
 <=====
 TTGATATTTTGATCAATTAATAATTATTCCGTAAACAGACACCAGCGCTACAGTACT
 3301 -----+-----+-----+-----+-----+-----+ 3360

=====
 CTTTAAAGAGTTACAGTAGTTTCGCTTCAAGATATTGAAAAGAATTAAACATTT
 3361 -----+-----+-----+-----+-----+-----+ 3420

TGAAAAAAAATCATCTAACATGTGCCAAACGCTTTCAAGTTCGCAGATTTTGA
 3421 -----+-----+-----+-----+-----+-----+ 3480

Repeat 2
 =====
 TTTTTTCATTCAAGATATGCTTATTAACACATATAATTATCATTAAATGTGAATTCTTG
 3481 -----+-----+-----+-----+-----+-----+ 3540

=====
 TAGAAATTTGGGCTTTCGTTCTAGTATGCTCTACTTTGAAATTGCTCAACGAAAAAA
 3541 -----+-----+-----+-----+-----+-----+ 3600

=====
 TCATGTGGTTGTTCATATGAATGACGAAAAATAGCAATTATATATTCCCCTAT
 3601 -----+-----+-----+-----+-----+-----+ 3660

=====
 TCATGTTGTGCAGAAAAATAGAAAAAGCGCATGCATTTCGACATTACATCGA
 3661 -----+-----+-----+-----+-----+-----+ 3720

=====>
 ACGACAGCTCACTCACATGCTGAAGACGAGAGACGCGGAGAAATACCACACATCTTCT
 3721 -----+-----+-----+-----+-----+-----+ 3780

Repeat 2
 <=====
 GCGTCTCTCGTCTTCAGCATGTGAAATGGGATCTCGGTCGATGTAAAAAAATGTCGAATA
 3781 -----+-----+-----+-----+-----+-----+ 3840

=====
 ATGTAAAAATGCATGCGTTTTACACTTTCTGCACAAATGAATAGGGGAAAATGT
 3841 -----+-----+-----+-----+-----+-----+ 3900

=====
 ATTAAAATACATTTTGATTTCAACATCACATGATTAACCCATTATTTTCGTT
 3901 -----+-----+-----+-----+-----+-----+ 3960

=====
 GAGCAACTAAAAAGTAGAGAATATTAGAGCGAAAACAAATTCTTCAAGATATTACC
 3961 -----+-----+-----+-----+-----+-----+ 4020

=====
 TTTATTGATAATTATAGATGTTAATAAGCATATCTTGAATGAAAGTCAGCAAAATATGT
 4021 -----+-----+-----+-----+-----+-----+ 4080

Fig. 3 (cont.)

4081 -----+-----+-----+-----+-----+-----+ 4140
 TTTTGCACTTCTACATCACATGAATGTAGAAAATTAAAAGGGAAATCAAAATTCTA
 4141 -----+-----+-----+-----+-----+-----+ 4200
 GAGGATATAATTGAATGAAACATTGCGAAATTAAAATGTGCGAACGTCAAAAAAGAGGA
 4201 -----+-----+-----+-----+-----+-----+ 4260

AATTGGGTATCAAAATCGATCCTAAACCAACACATTTCAGCATCCGCCAACTCTTCAT
 4261 -----+-----+-----+-----+-----+-----+ 4320
 S A N S S F
 180

TCACCGGATGCTCTCTCGGATACAGTTCAAGTCGTAATCGCTCATTAGCAAAGCTT
 4321 -----+-----+-----+-----+-----+-----+ 4380
 T G C S S L G Y S S S R N R S F S K A S
 190 200

CTGGACCAACTCAATAACATATTCCATGAAGAGGGATATGAACCTTGTGATGCACCAACCA
 4381 -----+-----+-----+-----+-----+-----+ 4440
 G P T Q Y I F H E E D M N F V D A P T I
 210 220

TAAGCCGTGTTTCGACGAGAAAACCATGTACAGAAACTTCTCGAGTCCTCGTGGAAATGT
 4441 -----+-----+-----+-----+-----+-----+ 4500
 S R V F D E K T M Y R N F S S P R G M C
 230 240

GCCTCATCATAAATAATGAACACTTGAGCAGATGCCAACACGGAATGGTACCAAGGCCG
 4501 -----+-----+-----+-----+-----+-----+ 4560
 L I I N N E H F E Q M P T R N G T K A D
 250 260

ACAAGGACAATCTTACCAATTGTTAGATGCATGGCTATACGGTTATTGCAAGGACA
 4561 -----+-----+-----+-----+-----+-----+ 4620
 K D N L T N L F R C M G Y T V I C K D N
 270 280

| intron 4

ATCTGACGGGAAGGGTACGGCGAAATTATATTACCCAAACGCGAAATTGCCATTTGCG
 4621 -----+-----+-----+-----+-----+-----+ 4680
 L T G R

Repeat 3

======>
 CCGAAAATGTGGCGCCCGGTCTGACACGACAATTGTGTTAAATGCAAAATGTATAAT
 4681 -----+-----+-----+-----+-----+-----+ 4740
 TTTGCAAAAACAAAATTGAACTTCCCGCGAAATTGATTACCTAGTTCGAAATTTC
 4741 -----+-----+-----+-----+-----+-----+ 4800
 GTTTTTCCGGCTACATTATGTGTTTTCTAGTTTCTATAATATTGATGTAAAAA
 4801 -----+-----+-----+-----+-----+-----+ 4860
 ACCGTTGTAATTTCAGACAATTTCGCATAAAAATTGATAGCACGAAATCAATT
 4861 -----+-----+-----+-----+-----+-----+ 4920
 TTCTGAATTTCAAAATTATCCAAAATTGCAAAATTAAAATTGTAAGGCAAC
 4921 -----+-----+-----+-----+-----+-----+ 4980

Fig. 3 (cont.)

GGTGTTCATGAAATGTATTTAAAAACTTAAAAACACTCCGGAAAGCAATAA
 4981 -----+-----+-----+-----+-----+-----+-----+ 5040
 AAATCAAAACAACGTACAATTCAAATTCAAAGTTATTCCGATTTGTTATTTG
 5041 -----+-----+-----+-----+-----+-----+-----+ 5100
 CAAAATTGAAAAATCATGAAGGATTAGAAAAGTTATAACATTTCTAGATTT
 5101 -----+-----+-----+-----+-----+-----+-----+ 5160
 TCAAAATTGTTAACAAATCGAGAAAAGAGAATGAAAATCGATTTAAAAATATCC
 5161 -----+-----+-----+-----+-----+-----+-----+ 5220

Repeat 3

<=====

ACAGCTTCGAGAGTTGAAATTACAGTACTCCTTAAAGGCGCACACCCATTGCATTGG
 5221 -----+-----+-----+-----+-----+-----+-----+ 5280

=====

ACCAAAAATTGCGTGTGAGACCAGGTACCGTAGTTTGTGCAAAATTGCAACCAT
 5281 -----+-----+-----+-----+-----+-----+-----+ 5340
 TGGACAATAAACCTTCTTAATCACCAAAAGTAAAATTGAAATCTCGAAAAGCCAAAA
 5341 -----+-----+-----+-----+-----+-----+-----+ 5400
 ATTCAAAAAAAAGTCGAATTCGATTTTTGGTTTTGGTCCCAAAACCAAA
 5401 -----+-----+-----+-----+-----+-----+-----+ 5460
 AAATCAATTCTGCAAAATACCAAAAGAAACCGAAAAATTCCCAGCCTGTTCT
 5461 -----+-----+-----+-----+-----+-----+-----+ 5520

AATGTAAACTGATATTAATTCCAGGGAATGCTCCTGACAATTGAGACTTGCCAAAC
 5521 -----+-----+-----+-----+-----+-----+-----+ 5580
 G M L L T I R D F A K H
 290 300

ACGAATCACACGGAGATTCTGCGATACTCGTATTCTATCACACGGAGAAGAGAATGTGA
 5581 -----+-----+-----+-----+-----+-----+-----+ 5640
 E S H G D S A I L V I L S H G E E N V I
 310 320

TTATTGGAGTTGATGATACCGATTAGTACACACGAGATATGATCTCTAACGCGG
 5641 -----+-----+-----+-----+-----+-----+-----+
 I G V D D I P I S T H E I Y D L L N A A
 330 340

A(n2433)
 | | intron 5

CAAATGCTCCCCGTCTGGCGAATAAGCCGAAATCGTTTGTGCAGGCTGTCGAGGCG
 5701 -----+-----+-----+-----+-----+-----+-----+ 5760
 N A P R L A N K P K I V F V Q A C R G E
 350 360

GTTCGTTTTATTTAATTTAATATAATTTAAATAATTCAAGAACGTC
 5761 -----+-----+-----+-----+-----+-----+-----+ 5820
 R R

GTGACAATGGATTCCCAGTCTGGATTCTGCGACGGAGTCTGCATTCTCGTCGTG
 5821 -----+-----+-----+-----+-----+-----+-----+ 5880
 D N G F P V L D S V D G V P A F L R R G
 370 380

Fig. 3 (cont.)

T (n1165)

GATGGGACAATCGAGACGGGCCATTGTTCAATTTCTTGGATGTGTGCGGCCGCAAGTTC
 5881 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 5940
 W D N R D G P L F N F L G C V R P Q V Q
 390 400

| intron 6

AGGTTGCAATTAAATTCTTGAATGAGAATATTCTTCAAAAAATCTAAAATAGATTTT
 5941 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 6000
 ATTCCAGAAAGTCCCGATCGAAAAATTGCGATATAATTACGAAATTGTGATAAAATGAC
 6001 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 6060

Repeat 4

AAACCAATCAGCATCGTCGATCTCCGCCACTTCATCGGATTGGTTGAAAGTGGCGGA
 6061 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 6120

===== >

GTGAATTGCTGATTGGTCGCAGTTTCAGTTAGAGGGAAATTAAAAATGCCCTTTCGA
 6121 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 6180
 AAATTAAAAATTGATTTTCATTTTCGAAAAATTCCGATTATTTATATTCTT
 6181 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 6240

A (n717)

GGAGCGAAAGCCCCGTCTGTAAACATTTAAATGATAATTAAATAATTGGCAGCAA
 6241 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 6300
 Q

T (n1949)

GTGTGGAGAAAGGCCGAGCCAAGCTGACATTCTGATTGATACGCAACGACAGCTCAA
 6301 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 6360
 V W R K K P S Q A D I L I R Y A T T A Q
 410 420

A (n1286)

TATGTTCTGGAGAACAGTGCTCGTGGATCATGGTCATTCAAGCCGTCTGTGAAGTG
 6361 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 6420
 Y V S W R N S A R G S W F I Q A V C E V
 430 440

T (n1129, n1164)

TTCTCGACACACGAAAGGATATGGATGTTGAGCTGCTGACTGAAGTCAATAAGAAG
 6421 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 6480
 F S T H A K D M D V V E L L T E V N K K
 450 460

T (n2430)

GTCGCTTGTGGATTCAGACATCACAGGGATCGAATATTTGAAACAGATGCCAGAGGTA
 6481 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 6540
 V A C G F Q T S Q G S N I L K Q M P E
 470 480

A (n2426)
| | intron 7

Fig. 3 (cont.)

Repeat 5

```

=====
6541 CTTGAAACAAACAATGCATGTCTAAGGACACAGAAAATAGGCAGAGGCTCCT 6600
       +-----+-----+-----+-----+-----+
===== >
6601 TTTGCAAGCCTGCCGCGCTAACCTAGAATTAGTTAGCTAAAATGATTGATT 6660
       +-----+-----+-----+-----+-----+
6661 GAATATTTATGCTAATTGGCGTTAAATTTGAAATAGTCACTATTATCGGGTT 6720
       +-----+-----+-----+-----+-----+
6721 CCAGTAAAAAATGTTATTAGCCATTGGATTACTGAAAACGAAAATTGAGTTTC 6780
       +-----+-----+-----+-----+-----+
6781 AACGAAATTATCGATTAAATGTAACGAAAATTACATCAACCATCAA 6840
       +-----+-----+-----+-----+-----+
6841 GCATTAAAGCCAAAATTGTTAACTCATTAAAAATTAAATTCAAAGTTGTCCACGAGTATT 6900
       +-----+-----+-----+-----+

```

Repeat 5

```

<=====
6901 ACACGGTTGGCGCGCGCAAGTTGCAAAACGACGCTCCGCCTTTCTGTGCGGCTT 6960
       +-----+-----+-----+-----+-----+

```

T(n1163)

```

=====
6961 GAAAACAAGGGATCGGTTAGATTTCCCAAAATTAAATTAAATTCAAGATGACATC 7020
       +-----+-----+-----+-----+-----+
       |   |   |   |
       M   T   S

```

CCGCCTGCTAAAAAGTTCTACTTTGCCGGAAGCACGAAACTCTGCCGTCTAAAATTC 7080

```

7021 R   L   L   K   K   F   Y   F   W   P   E   A   R   N   S   A   V   *
       490           500
ACTCGTGATTCAATTGCCAATTGATAATTGCTGTATCTTCTCCCCAGTTCTCTTCGC 7140
7081 CCAATTAGTTAAACCATGTGTATATTGTTATCCTACTCATTCACTTATCATTCT
7141 ATCATTCTCTCCATTTCACACATTCCATTCTCTACGATAATCTAAAATTATGAC 7200
7201 GTTTGTGTCTCGAACGCATAATAATTAAACTCGTTGAATTGATTAGTTGTTGT 7260
7261 GCCCAGTATATATGTACTATGCTTCTATCAACAAAATAGTTCATAGATCATCACC 7320
7321 CCAACCCCACCAACCTACCGTACCATATTCAATTGGCCGGAAATCAATTGATTAATT 7380
7381 TTAACCTATTTCGCCACAAAAATCTAATATTGAATTAAACGAATAGCATTCCCATC 7440
7441 TCTCCCGTGCCGGAATGCCTCCGGCTTTAAAGTTCGGAACATTGGCAATTATGTAT 7500
7501 AAATTGTAGGTCCCCCCCATTCTCCGCCATCATCTCAAATTGCATTCTTTTCG 7560
7561 CCGTGATATCCCGATTCTGGTCAGCAAAGATCT 7620
7621 7653

```

Fig. 3 (cont.)

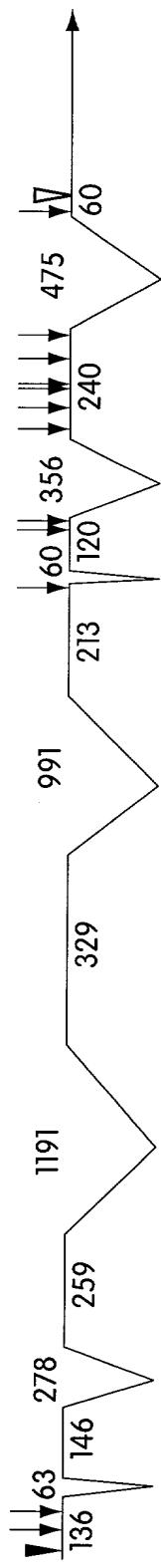


Fig. 4A

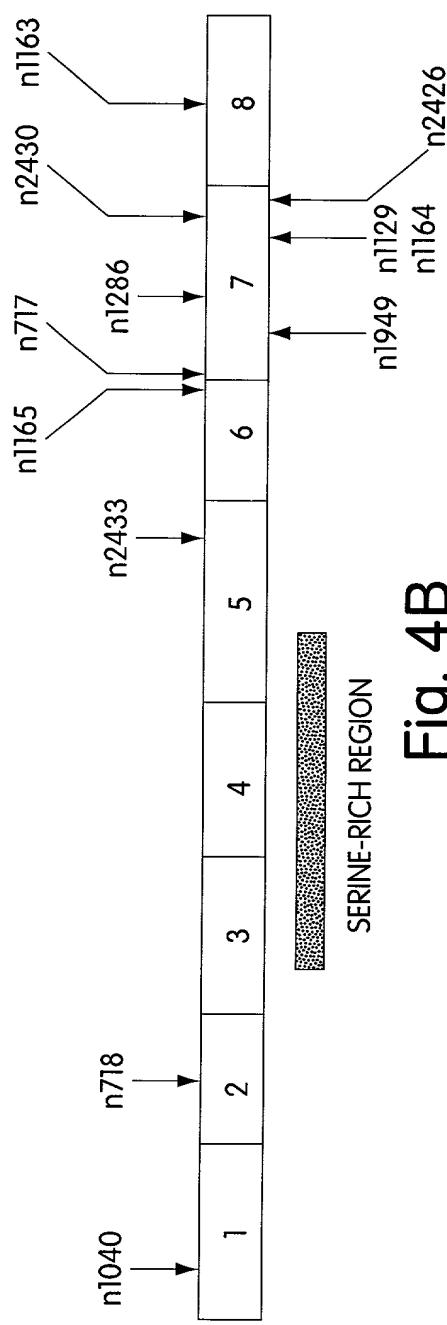


Fig. 4B

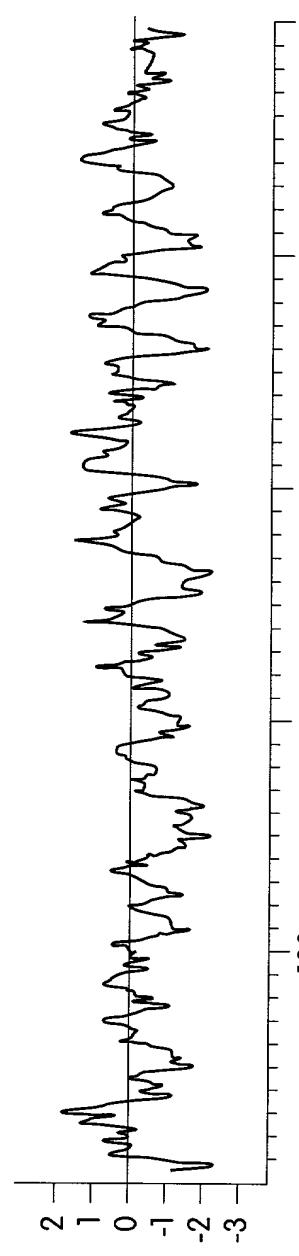


Fig. 5

Alignment of ced-3 and Human Interleukin -1 β convertase

| | | |
|-------|---|--|
| ICE | 1 | MADKVLKEKRKLFIRSM....GEGTINGLLDELLQTRVLNKEEMEKVKRE .. :: .: ..: ..:.. . .::: : :... ..:::.. . . |
| Ced-3 | 1 | ...MMRQDRRSLLERNIMMFSSHLKVDEILEVLIAKQVLNSDNGDMIN.S |
| | | ↓ F |
| BGAFQ | | ===== |
| PBA | | ===== |

| | |
|-------|--|
| 47 | NATVMDKTRALIDSVIPKGAQACQ. ICITYICEEDSYLAGTLGLSADQTS : .: .:... : :: .. :.... :.. : .. |
| 47 | CGTVREKRREIVKAVQRPGDVAFDAFYDALRSTGHEGLAEVLEPLARSVD ↓ R |
| BFAFQ | ===== |
| PBA | ===== |

| | | |
|-------|--|---------------------|
| | | autocleavage site |
| 96 | GNYLNMQ..... |DSQGVLSFF..... |
| | : : :: : | : |
| 97 | SNAVEFECPMSPASHRRSRALSPAGYTSPTRVHRDSVSSVSSFTSYODIY | serine-rich region |
| BGAFQ | ===== | ===== |
| PBA | ===== | ===== |

| | |
|-----|--|
| 112 | PAPQAVQDNPAMPTSSGSEG NVKLC SLE |
| | : : : . |
| 147 | <u>SRARSRSRSRALHSSDRHNYSSPPVNAFPSOPSSANSFTGCSSLGYSSS</u> |

140 EAQRIWKQKSAEIYPIMDK..... SSRTRLAL
.....|..... | : ..| ||. :.|
197 RNRFSKASGPTQYIFHEEDMNFDAPTISRVDDEKTMYRNFSSSPRGMCL
BGAFO =====

Fig. 6A

ICE 167 IICNEEFDSIPRRTGAEVDIRGMTMLLQNLGYSDVKKNLTASDMTTELE
 || ||.:: :| .|...| ...| || .::||. .| .||::| ..
 Ced-3 247 IINNEHFEQMPTRNGTKADKDNLTNLFRCMGTICKDNLTGRGMLLTIR
 BGAFQ =====

217 AFAHRPEHKTSDSTFLVFMSHGIREGICGKKHSEQVPDI.LQLNAIFNML
 .||.:.| :||.::||| .|.|| : .||: .::|:
 297 DFAKHESH..GDSAILVILSHGEENVIIG.....VDDIPISTHEIYDLL
 BGAFQ =====

active site autocleavage site
 266 NTKNCPSLKDPKVIIIQACRGDSPGVWW.FKDSVGVSGNLSLPTTEFE
 |. .|.| :||:::||| .: .|||: . .: .|||: . .: .|||:
 339 NAANAPRLANKPKIVFVQACRGERRDNGFPVLDSDGVPAFLRRGWDNRD
 ↓
 S
 BGAFQ =====

315 DDAI.....KKAHIEKDFIAFCSSPDNVSWRHPTMGSVFI
 .. : .| .: .|||: . .: .|||: . .: .|||:
 389 GPLFNFLGCVRPQQVWRKKPSQADILIRYATTAQYVSWRNSARGSWFI
 ↓ stop ↓ stop
 stop

351 GRLIEHMQEYACSCDVEEIF....RKVRFSFEQPDGRAQMPTT.ERVTL
 . .:| : ..| .|||: .|||: .|||: . .: .|||:
 439 QAVCEVFSTHAKDMDVVELTEVNKKVACGFQTSQGSNILKQMPPEMTSRL
 ↓ V ↓ V ↓ K ↓ F

395 TRCFYLFPGH*.... 404
 : ||::|:
 489 LKKFYFWPEARNSAV 503

Fig. 6A (cont.)

Alignment of Ced-3 and Murine NEDD-2

| | | |
|-----|--------|-----|
| 499 | RNSAV | 503 |
| 169 | PPT... | 172 |

6GB
Foto

Alignment of N-terminal regions of ced-3/ICE- related proteins

| | | |
|-------------------|---|-----|
| c. briggsae ced-3 | MMRQDRWILLERNILEFSSSKLLOADLILDLIAKQVILNSDNGDVINSCRTERNEKEIVKAVQRGDEAFDAFYDALRDTGNDLADVLMLPLSR---PNPV | 100 |
| ced-3 protein | MMRQDRRSLLERNTIMMFSSSHLYKVEILLEVLIAKQVILNSDNGDMINSCGTYREKREITKAVQRPQDVAFDAAFYDALRSTGHEGLAEVLEPLARSVDNAV | |
| C.vulgaris ced-3 | M-----ADKIL-----RAKRQFINSV-----SIGHTLDELLEK-----RVLNQEM-----DKI | |
| Mouse ICE.gw | M-----ADKVL-----REKRLFIRSM-----GETTINGLLELLQT-----RVLNKEEM-----EKV | |
| Human ICE.GW | | |
| Consensus | M.....AD..IL.....R.KRK.....V...G.....D.I..T.....VL.....V | |
| c. briggsae ced-3 | PMECPMSPSSHRRRSRALSPPGYASPTRVHRDSTISSFTSTYQDVYSRARSSSSRPLQSSDRHNTMSAA-TSEPSQSSANSSETGCAASLGYSSSRN | 198 |
| ced-3 protein | EFECPMSPASHRRRSRALSPAGTSPTRVHDSSVSSSFTSYQD-TYSRAPSRSRSRS-RALHSSDRHNTSSPPVMAPSQPSANSSETGCGSSLGYSSSRN | |
| C.vulgaris ced-3 | M-----STSSRSPRHTSDRHNTVSPS-NSFQSQPASANSSETGCGSSLGYSSSRN | |
| Mouse ICE.gw | KLA---NITAMDKARDLICDHDVSKKGQASQIIFTYICNEDCYL-----AGILEQOSAPSAE-TFVAT-----EDSKGGHPSISSETKEQNKED-G | |
| Human ICE.GW | KRE---NATVMDKTRALIDSVIPKGAQACQICITYICEEDSYL-----ACTLGLSADQTSG-NYLNM-----QDSQGVLSSTFPAPQAVQDNFAMP | |
| Consensus | ..E----.RAL.....I.....SY.....I.....S.SRS.R.L.SSDRHNYS...F.SQP.SANSSSFTG.-SLGYSSSR. | |
| c. briggsae ced-3 | RSFSKTSAQSQYIIFHEEDMIVDAPTIHRVFDKTMYRNFSSPRGQLIINNEHETEQMPTTRNGTKAKDKDNLTNITRCMGTYVICKDNLTGRELSTIRSF | 298 |
| ced-3 protein | RSFSKASGPTQYIIFHEEDMIVDAPTIISRVFDEKTMYRNFSSPRGQLIINNEHETEQMPTTRNGTKAKDKDNLTNITRCMGTYVICKDNLTGRELSTIRDF | |
| C.vulgaris ced-3 | RSYSKASAHSQYIIFHEEDMIVDAPTIHRVFDKTMYRNFSSPRGQLIINNEHETEQMPTTRNGTKPKDNLTNITRCMGTYVICKDNLTGRELSTIRDF | |
| Mouse ICE.gw | TFPGILTGTIKFCPLEXAQKLMKENPS--EY--PIMMTT-TRTR-LAIIIONTFQHLSPRVGAQVDTREMKLILEDIGTYVICKENLTIALEMVKREVKEF | |
| Human ICE.GW | TSSSEGNVKLCSLEEAQRIWKQSA--EY--PIMDKS-SRTR-LAIIIONNEEDTSIPRTTGAEVDTGTMILQLQNLGYSDYTKKNTIASDMTTELEAF | |
| Consensus | RS .SK .S .QYIIFHEEDMIVDAPTI .RVFDEKTMYRNFSSPRGQLIINNEHETEQMPTTRNGTK .DKDN .TNLFRCMGTY .CKDNLTG .ML .TIR .E | |
| c. briggsae ced-3 | GRNDME-GDSAIITVTLISHGEENVITG--VDDVS--VNVEHEITDILNAANAPRILANKPKLVLVFOACRG | 360 |
| ced-3 protein | AKHESH--GD SAIITVTLISHGEENVITG--VDDIP--ISTHEIYDILNAANAPRILANKPKLIVFVFOACRG | |
| C.vulgaris ced-3 | AKNETH--GD SAIITVTLISHGEENVITG--VDDVS--VNVEHEITDILNAANAPRILANKPKLIVFVFOACRG | |
| Mouse ICE.gw | AACPEEKTKTSDSTFLVEMSHGQI QEGICGTTYSNEVSDILKVDTIFQMMNTLNCPSLKDQPKVIIQACRG | |
| Human ICE.GW | AHRPEEKTKTSDSTFLVEMSHGQI QEGICGTTYSNEVSDILKVDTIFQMMNTLNCPSLKDQPKVIIQACRG | |
| Consensus | A....H .CDSAIITVTLISHGEENVITG--VDDVS--.VHEIYDILNAANAPRILANKPKLVLVFOACRG | |

15/24

Fig. 6C

Alignment of C-terminal regions of ced-3/ICE/NEDD-2 - related proteins

| | | | | | | | |
|------------------------|--|-----------|-------------------------------------|-------------|-----------------|-------|-----------------|
| ICE C-terminus | DSPGVVVW---- | ----- | -FDGSVG-- | ----- | ----- | ----- | ----- |
| Mouse ICE C-ter | EKQGVVL----- | ----- | -----LKDSVR----- | ----- | ----- | ----- | -----D |
| C.briggsae C-ter | ERRDNGFP----- | ----- | -----VLDSDVGD----- | ----- | -----VPSLI----- | ----- | -----RRGWDN |
| ced-3 C-terminus | ERRDNGFP----- | ----- | -----VLDSDVGD----- | ----- | -----VPAFL----- | ----- | -----RRGWDN 386 |
| C. vulgaris C-terminus | ERRDVGFP----- | ----- | -----VLDSDVGD----- | ----- | -----VPALI----- | ----- | -----RRGWDK |
| nedd-2 protein.gw | MLTVQVYRTS QKCSSSSKTVV | EVLDPLGTS | FCSLLPPPLI LYETDRGVDQ | | | | |
| Consensus | E..... | |LDSV..... |P..... |RG.D. | | |
| ICE C-terminus | SGNL---SIP TIEEE-----D DAIKKA-HIE KDFIAFCSSST PDNIVSMWHPHT | | | | | | |
| Mouse ICE C-ter | SEE----DFL TDAIPE---D DGIKKA-HIE KDFIAFCSSST PDNIVSMWHPV | | | | | | |
| C.briggsae C-ter | RDG-PLFNFQ GCVRFQV--Q QVWRKK-PSQ ADMLIAYATT AQYVSMWNSA | | | | | | |
| ced-3 C-terminus | RDG-PLFNFQ GCVRFQV--Q QVWRKK-PSQ ADMLIAYATT AQYVSMWNSA 432 | | | | | | |
| C. vulgaris C-terminus | GDG-P--NFL GCVRFQA--Q QVWRKK-PSQ ADMLIAYATT AQYVSMWNSA | | | | | | |
| nedd-2 protein.gw | QDGKNAHTQSP GCEESDAGKE ELMKMRLLPTR SDMICGYACL KGNAAMRNTK | | | | | | |
| Consensus | .DG----FL GC..... | |K.-P...D.....YA.T.....VSWRN... | | | | |
| ICE C-terminus | MGSVFTIGRLI EHMQEYACSC DVEEIRKAV-----RF-----SFE QPDGCAQMPT | | | | | | |
| Mouse ICE C-ter | RGSLSLFIESTLII KHMKEYIAWSC DILEDIFRAV-----RF-----SFE QPEERLQMP | | | | | | |
| C.briggsae C-ter | TGSWFTIQAVC EVFSLHAKDM DVVELLTEVN KKVA--CGFQ TSQGSNILKQ | | | | | | |
| ced-3 C-terminus | TGSWFTIQAVC EVFSTHAKDM DVVELLTEVN KKVA--CGFQ TSQGSNILKQ 480 | | | | | | |
| C. vulgaris C-terminus | TGSWFTIQAVC EVFSLHAKDM DVVELLTEVN KKVA--CGFQ TSQGSNILKQ | | | | | | |
| nedd-2 protein.gw | TGSWFTIQAVC EVFSLHAKDM DVVELLTEVN KKVA--CGFQ TSQGSNILKQ | | | | | | |
| Consensus | RGS.FI.A... EVFS...A.DM DV.E.L.V.GF...G....K. | | | | | | |
| ICE C-terminus | T-ERVLTTR CFYLFPGH----- | | | | | | |
| Mouse ICE C-ter | A-DRVTLTK RFLYLFPGH----- | | | | | | |
| C.briggsae C-ter | MPELTTSRLIK KFYFWPEDRG RNSAV | | | | | | |
| ced-3 C-terminus | MPEMTTSRLIK KFYFWPEAR- -NSAV 503 | | | | | | |
| C. vulgaris C-terminus | MPELTTSRLIK KFYFWPEDRN RSSAV | | | | | | |
| nedd-2 protein.gw | MSEYCSTLICQ QLYLFPG--- -YPTT | | | | | | |
| Consensus | M.E...S.L.K .FY...P...- - - | | | | | | |

Fig. 6D

Lines

1 01 MMRQDRRSLLERNIMMFSSHLKVDEILEVLIAKQVLNSDNGDMINSCGT 50
 2W.....LE...K.QA.L..D.....V....R.E
 3 TVSISLI..R..... M.....

1 51 REKRREIVKAVQRPGDVAFDAFYDALRSTGHEGLAEVLEPLARSVDSNAV 100
 2 .DNEK.....R..E.....D...ND..D..M..S.P .P.
 3

1 101 EFECPMSPASHRRSRALSPAGYTSPTRVHRDSVSSVSSFTS YQDIYSRA 149
 2 PM.....S.....P .A.....I.....T...V....
 3 S

1 150 RSRSR_SRALHSSDRHNYSSPPVNAFPSQPSSANSFTGCSSLGYSSSRN 198
 2 ..S..S..P.Q.....M.AA_TS..... A.....
 3 T..._P..T.....V..S..S.Q..A.....S.....T

1 199 RSFSKASGPTQYIFHEEDMNFDAPTISRVFDEKTMYRNFSPPRGMCLI 247
 2T.AQS.....Y.....H.....L...
 3 ..Y....AHS.....Y.....H.....T...L...

1 248 INNEHFEQMPTRNGTKADKDNLTNLFRCMGYTVICKDNLTGRGMLLTIRD 297
 2I.....E..S...S
 3P....IS.....I.H..... M.....

1 298 FAKHESHGDSAILVILSHGEENVIIIGVDDIPISTHEIYDLLNAANAPRLA 347
 2 .GRNDM..... VSVNV.....
 3 ...N.T..... VSVNV....X.....

1 348 NPKIIVFVQACRGERRDNGFPVLDSVDGVPAFLRRGWDNRDGPLFNFLGC 397
 2L.....SLI.....
 3L.....V.....LI....KG...

1 398 VRPQQVWRKKPSQADILIRYATTAQYVSWRNSARGSWFIQAVCEVFST 447
 2M..A.....L
 3A.....A.....L

1 448 HAKDMVVELLTEVNKKVACGFQTSQGSNILKQMPMTSRLKKFYFWPE 497
 2L.....
 3A..... L.....

1 498 ARN SAV 503
 2 DRG...
 3 D..RS...

Interleukin-1 β convertase cDNA sequence

1 AAAAGGAGAG AAAAGCCATG GCCGACAAGG TCCTGAAGGA GAAGAGAAAG
 51 CTGTTTATCC GTTCCATGGG TGAAAGGTACA ATAAATGGCT TACTGGATGA
 101 ATTATTACAG ACAAGGGTGC TGAAACAAGGA AGAGATGGAG AAAGTAAAAC
 151 GTGAAAATGC TACAGTTATG GATAAGACCC GAGCTTGAT TGACTCCGTT
 201 ATTCCGAAAG GGGCACAGGC ATGCCAAATT TGCATCACAT ACATTTGTGA
 251 AGAAGACAGT TACCTGGCAG GGACGCTGGG ACTCTCAGCA GATCAAACAT
 301 CTGGAAATTA CCTTAATATG CAAGACTCTC AAGGAGTACT TTCTTCCTT
 351 CCAGCTCCTC AGGCAGTGCA GGACAACCCA GCTATGCCA CATCCTCAGG
 401 CTCAGAAGGG AATGTCAAGC TTTGCTCCCT AGAAGAAGCT CAAAGGATAT
 451 GGAAACAAAAA GTCGGCAGAG ATTTATCCAA TAATGGACAA GTCAAGCCGC
 501 ACACGTCTTG CTCTCATTAT CTGCAATGAA GAATTTGACA GTATTCTAG
 551 AAGAACTGGA GCTGAGGTTG ACATCACAGG CATGACAATG CTGCTACAAA
 601 ATCTGGGTA CAGCGTAGAT GTGAAAAAAA ATCTCACTGC TTCGGACATG
 651 ACTACAGAGC TGGAGGCATT TGCACACCGC CCAGAGCACA AGACCTCTGA
 701 CAGCACGTTTC CTGGTGTCA TGTCTCATGG TATTGGGAA GGCATTGTG
 751 GGAAGAAACA CTCTGAGCAA GTCCCAGATA TACTACAATC CAATGCAATC
 801 TTTAACATGT TGAATACCAA GAACTGCCA AGTTGAAGG ACAAAACGAA
 851 GGTGATCATC ATCCAGGCCT GCCGTGGTGA CAGCCCTGGT GTGGTGTGGT
 901 TTAAAGATTC AGTAGGAGTT TCTGGAAACC TATCTTACCA AACTACAGAA
 951 GAGTTTGAGG ATGATGCTAT TAAGAAAGCC CACATAGAGA AGGATTTAT
 1001 CGCTTCTGC TCTTCCACAC CAGATAATGT TTCTGGAGA CATCCCACAA
 1051 TGGGCTCTGT TTTTATTGGA AGACTCATTG AACATATGCA AGAATATGCC
 1101 TGTTCTGTG ATGTGGAGGA AATTTCCGC AAGGTTCGAT TTTCATTTGA
 1151 GCAGCCAGAT GGTAGAGCGC AGATGCCAC CACTGAAAGA GTGACTTTGA
 1201 CAAGATGTTT CTACCTCTTC CCAGGACATT AAAATAAGGA AACTGTATGA
 1251 ATGTCTGCGG GCAGGAAGTG AAGAGATCGT TCTGTAAAAG GTTTTGAA
 1301 TTATGTCTGC TGAATAATAA ACTTTTTTG AAATAATAA TCTGGTAGAA
 1351 AAATGAAAAA AAAAAAAA AAA

Fig. 8

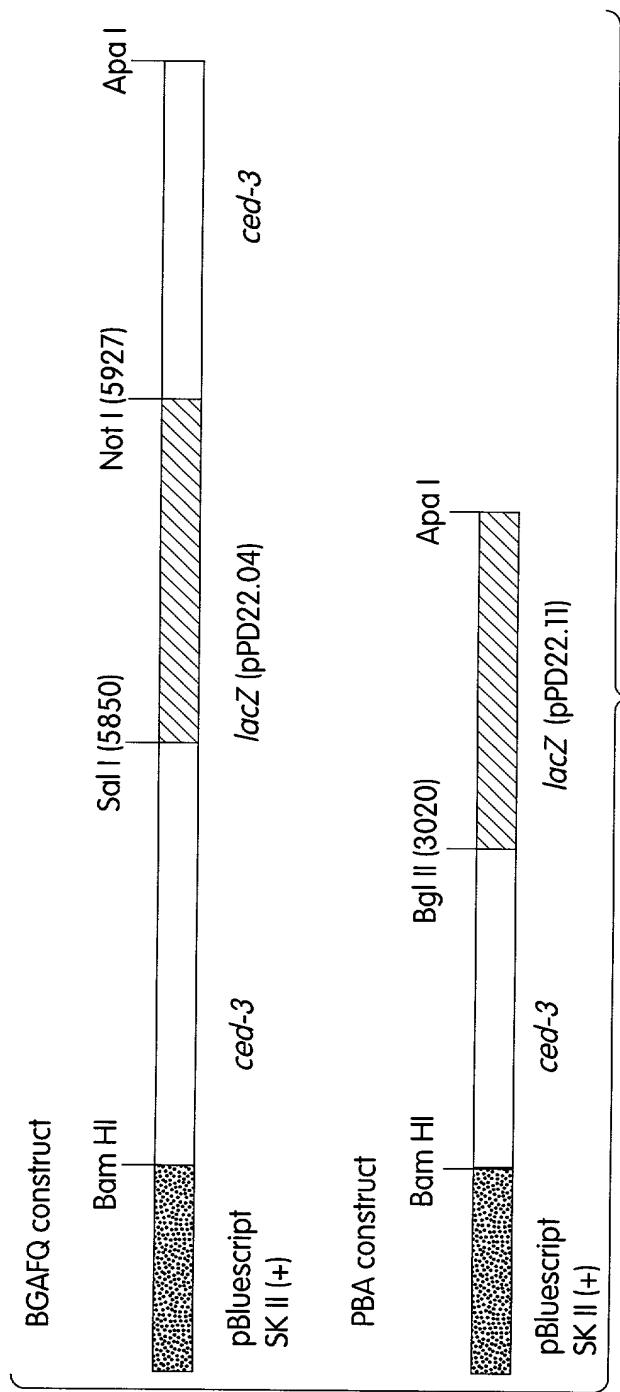


Fig.9A

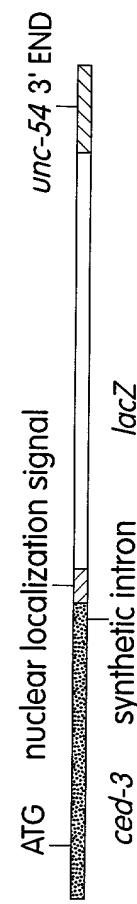


Fig.9B

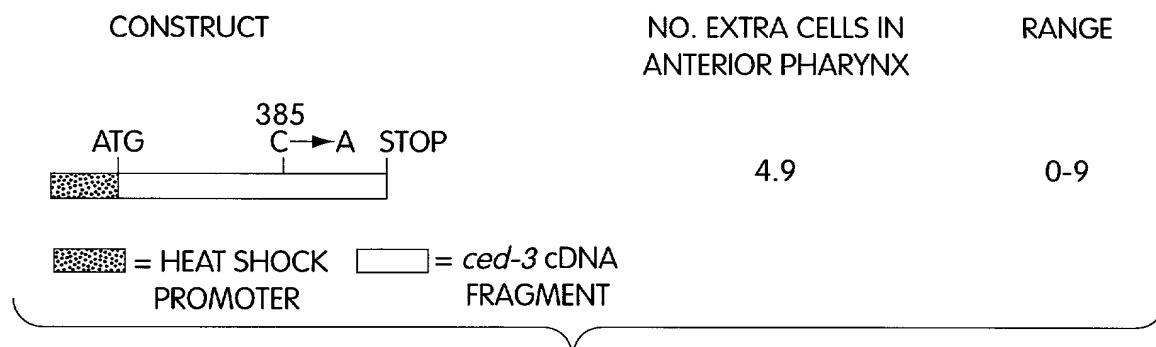


Fig. 10

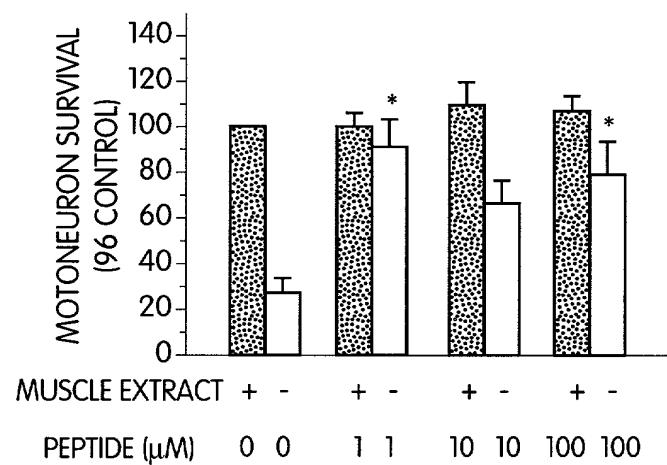


Fig. 11A

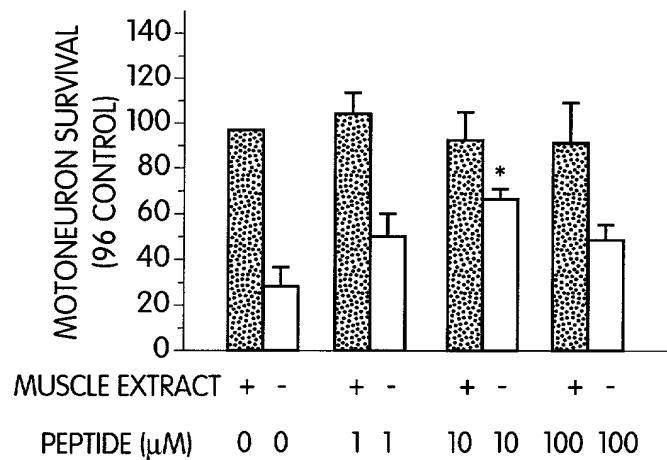


Fig. 11B

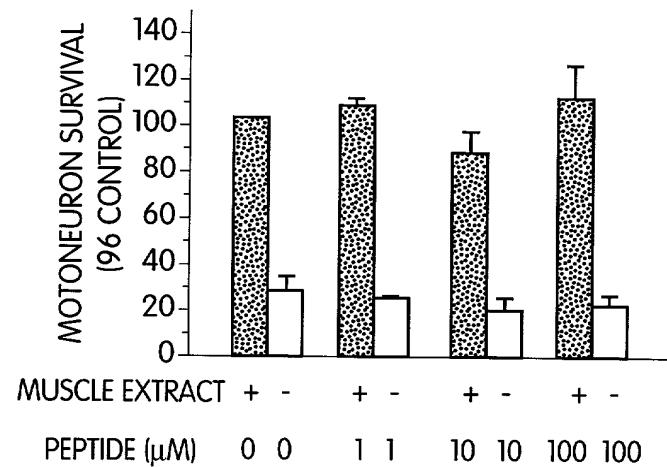


Fig. 11C

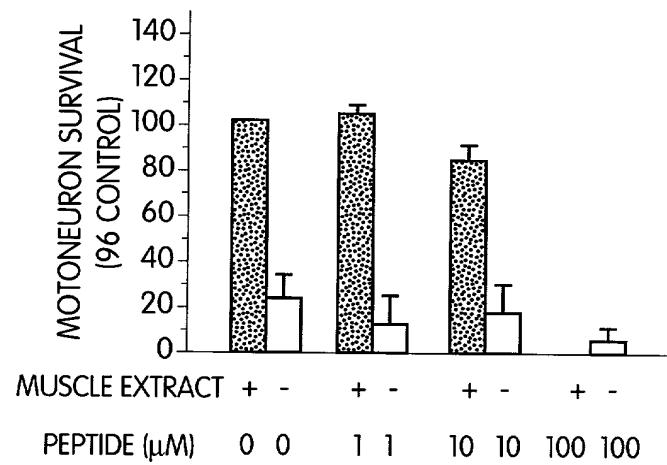


Fig. 11D

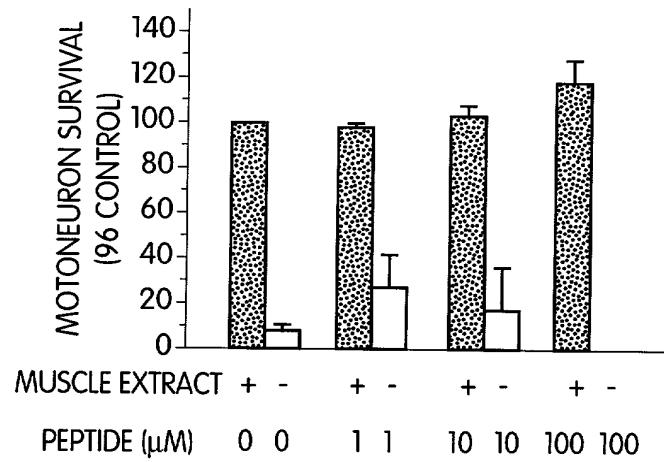


Fig. 11E

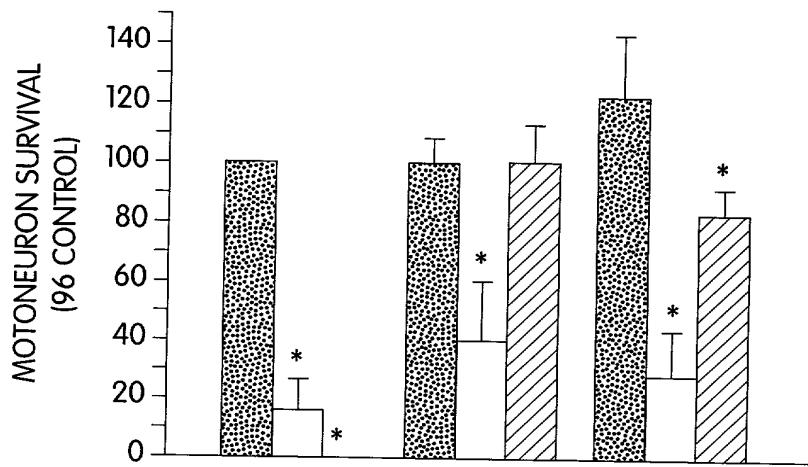


Fig. 12A

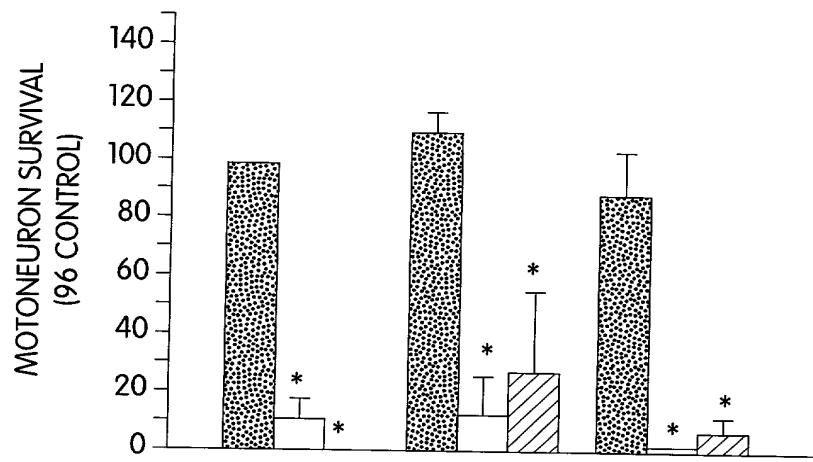


Fig. 12B

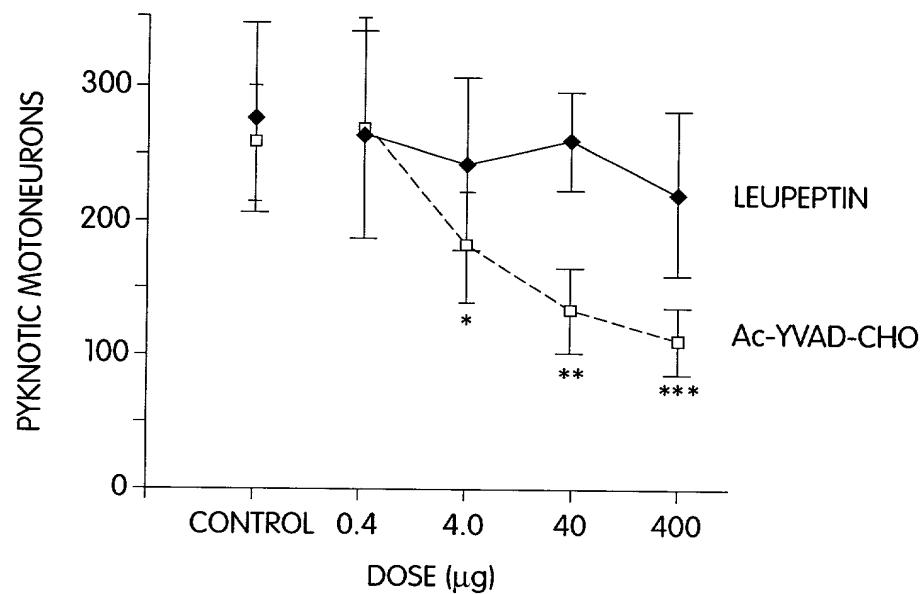


Fig. 13

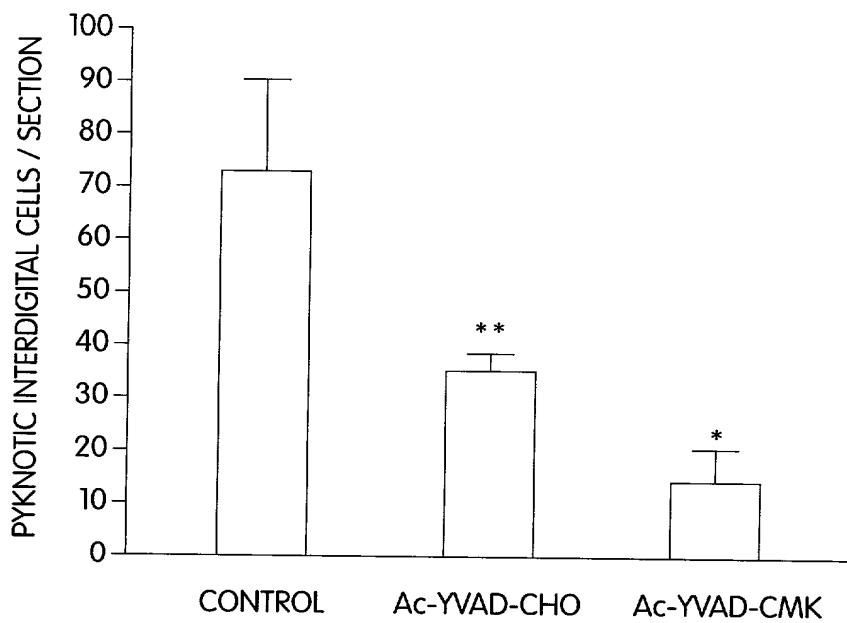


Fig. 14

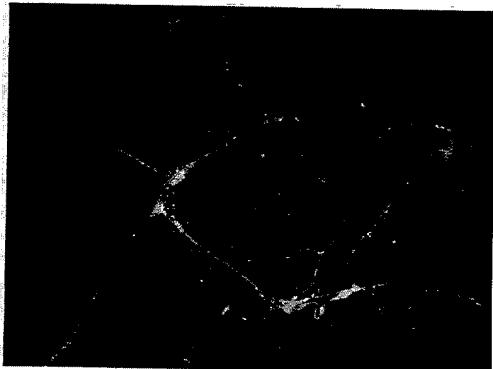


Fig. 15C



Fig. 15D

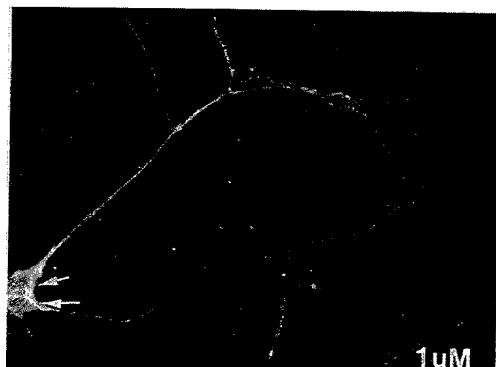


Fig. 15E



Fig. 15F



Fig. 15G